

What is claimed is:

1. A method for treating diabetes mellitus in an individual in need thereof, said method comprising:

5 administering to said individual a composition providing at least one receptor ligand selected from the group consisting of a gastrin/CCK receptor ligand and an EGF receptor ligand in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells.

10 2. The method according to Claim 1, wherein said at least one receptor ligand is an EGF receptor ligand selected from the group consisting of EGF1-53, EGF1-48, or its EGF1-47 or EGF1-49 congener.

15 3. The method according to Claim 2, wherein said EGF1-53, EGF1-48, or its EGF1-47 or EGF1-49 congener is human EGF1-53, EGF1-48, or its EGF1-47 or EGF1-49 or its congener.

20 4. A method for providing a patient with diabetes in need thereof with a population of mature insulin-secreting beta cells, said method comprising:

transplanting into said patient cultured pancreatic islets which have been provided with a sufficient amount of at least one receptor ligand selected from the group consisting of a gastrin/CCK receptor ligand and an epidermal growth factor receptor ligand to induce proliferation of mature insulin-secreting beta cells of said islets prior to said transplanting.

25 5. The method according to Claim 4, wherein said diabetes is Type 2 diabetes.

6. The method according to Claim 4, wherein said gastrin/CCK receptor ligand is a gastrin.

30 7. The method according to Claim 4, wherein said epidermal growth receptor ligand is TGF- $\alpha$  or an EGF selected from the group consisting of EGF1-53, EGF1-48, or its EGF1-47 or EGF1-49 congener.

8. A method for expanding a population of pancreatic beta cells, said method comprising:

providing said pancreatic beta cells with a sufficient amount of a gastrin/CCK receptor ligand and an epidermal growth factor receptor ligand to induce proliferation of said pancreatic beta cells, whereby an expanded population of pancreatic beta cells is obtained.

9. A composition comprising:

pancreatic  $\beta$  cells, wherein said culture is obtained by providing pancreatic islets with a sufficient amount of a gastrin receptor agonist and an epidermal growth factor receptor agonist to induce proliferation of said pancreatic  $\beta$  cells.

10. A method for treating diabetes in an individual in need thereof, said method comprising:

administering to said individual a composition comprising at least one receptor ligand selected from the group consisting of a proteinaceous gastrin/CCK receptor ligand and a proteinaceous EGF receptor ligand in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells, wherein said composition is administered systemically.

11. The method according to Claim 10, wherein said proteinaceous gastrin/CCK receptor ligand is a gastrin.

12. The method according to Claim 10, wherein said proteinaceous EGF receptor ligand is a TGF- $\alpha$ .

13. The method according to Claim 10, wherein said diabetes is type 2 diabetes.

14. A method for stimulating pancreatic islet cell neogenesis in an individual in need thereof, said method comprising:

administering to said individual a composition comprising at least one receptor ligand selected from the group consisting of a gastrin/CCK receptor ligand and an EGF

receptor ligand in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting islet cells, wherein said composition is administered systemically.

- 5 15. The method according to Claim 14, wherein said individual.
16. The method according to Claim 14, wherein both said gastrin/CCK receptor ligand and said EGF receptor ligand are administered.
- 10 17. The method according to Claim 16, wherein at least one of said gastrin/CCK receptor ligand and said EGF receptor ligand is a proteinaceous receptor ligand.
- 15 18. A method for treating diabetes mellitus in an individual in need thereof which comprises administering to the individual a composition providing a gastrin/CCK receptor ligand and an EGF receptor ligand in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells.